REMARKS

I. Formal Matters

The Examiner objects to the language of the Abstract because it allegedly uses "legal phraseology." (Office Action, p. 2). The Abstract has been amended to remove the phrase "said method comprising." Applicants believe the amended Abstract overcomes the Examiner's objection.

The Examiner objects to claim 44 based on a misspelled word. *See id.* As discussed below, claim 44 has been canceled. Thus, the Examiner's rejection to claim 44 is moot.

Though not objected to, Applicants have noted that claim 37 incorrectly depends from itself. Accordingly, claim 37 has been amended to depend from claim 36 instead of from claim 37.

II. The Claims are Enabled

The Examiner rejects claims 36, 37, and 39-44 under 35 U.S.C. § 112, first paragraph, as allegedly being non-enabled. (*See* Office Action, p. 3). In particular, the Examiner claims that the specification does not teach one of skill in the art how to make and use adenoviruses lacking ITRs or an encapsidation signal, all "therapeutic" genes, and genes not operably linked to a promoter within the context of the present invention. (*See* Office Action, pp. 3-9). The Examiner further asserts that the specification is not enabling with respect to defective recombinant adenoviruses that are not of human or canine origin. (*See* Office Action, pp. 5-7).

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Without acquiescing in the rejection, and solely to advance prosecution, Applicants have amended independent claims 36 and 39 to recite that the adenoviruses are of human or canine origin, contain a left and right ITR, as well as an encapsidation signal, and comprise a suicide gene operably linked to a promoter. The Examiner acknowledges that the specification discloses defective adenovirus vectors that comprise a suicide gene operably linked to a promoter. (*See* Office Action, pp. 3 and 5). The Examiner further indicates that the rejected claims would be enabled if they are amended to include left and right ITR sequences, as well as a encapsidation signal, and if the adenoviral vectors are of canine or human origin. (See Office Action, pp. 4-9). Accordingly, since claims 36 and 39 have been amended to include these elements, Applicants believe the Examiner's enablement rejections have been overcome.

Since the limitations of dependent claims 38 and 40 have been incorporated into independent claims 36 and 39, respectively, claims 38 and 40 have been canceled. Since Applicants have canceled claims 41-44, the Examiner's rejection of those claims is moot. Accordingly, Applicants respectfully request that the rejection of the remaining claims 36, 37, and 39 under 35 U.S.C. § 112, first paragraph, be withdrawn.

III. The Claims Are Not Anticipated

The Examiner rejects claim 39 under 35 U.S.C. § 102(e) as allegedly being anticipated by French *et al.* (U.S. Patent No. 6,290,949). (*See* Office Action, p. 10). According to the Examiner, French *et al.* discloses a hydrogel-coated ballon catheter where the hydrogel is impregnated with an adenovirus containing a therapeutic gene

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that inhibits the decrease in luminal diameter of the artery. *Id.* The Examiner indicates that this rejection will be overcome by limiting claim 39 to a suicide gene, which is not disclosed in French *et al.* *Id.*

As discussed above, claim 39 has been amended to recite a suicide gene, as opposed to a "therapeutic" gene. Accordingly, Applicants believe that claim 39 is not anticipated by French *et al.* and respectfully request that the rejection of claim 39 under 35 U.S.C. § 102(e) be withdrawn.

IV. The Claims Are Not Obvious

The Examiner also rejects claims 36-40 under 35 U.S.C. § 103 as allegedly being unpatentable over Ohno *et al.* (*Science* 265:781-784 (1994)) in view of either Steg *et al.* (*Circulation* 88:1-660 (1993) ("Steg I"), or Steg *et al.* (*Circulation* 90:1648-1656 (1994)) ("Steg II"). (*See* Office Action, p. 11). According to the Examiner, Ohno describes a method for delivering a replication defective adenovirus comprising a left and right ITR, an encapsidation signal, and a suicide (TK) gene under the control of a promoter that functions in arterial vascular smooth muscle cells using an uncoated double balloon cathether. *Id.* The Examiner acknowledges, however, that Ohno fails to disclose delivery using a balloon catheter coated with an adenovirus-impregnated hydrogel. *Id.* To account for this deficiency, the Examiner relies on Steg I and Steg II. According to the Examiner, Steg I and Steg II report that the efficiency of adenovirus infection into smooth muscle cells may be increased by using a hydrogel-coated balloon catheter, rather than an uncoated catheter. Applicants respectfully traverse.

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Based on the foreign priority document for this application (FR 94/10083, filed August 17, 1994), the Steg II reference is not prior art to the instant invention since it has a publication date of October 1994, which is later than the filing date of the foreign priority document. A copy of the French priority document (FR 94/10083), along with a certified translation will be submitted once the translation is completed. Applicants respectfully request that the Examiner hold the rejection based on Steg II in abeyance until the certified translation of the priority document has been completed and submitted.

Although the Examiner asserts that the elements of claims 36-40 are found in prior art references, he has failed to show a motivation to combine these elements since there is no reasonable expectation of success in using the resulting combination. The claims of the present invention are directed to compositions, and catheter devices used to deliver these compositions, that comprise a recombinant adenovirus that contains a suicide gene useful for inhibiting a decrease in luminal diameter of an atheromatous blood vessel. Significantly, in the parent case to the present application (U.S. Application No. 08/633,769 - now U.S. Patent No. 6,410,011 - the '011 patent), the Examiner acknowledged that claims directed to methods of inhibiting a decrease in luminal diameter of an atheromatous blood vessel by administering the recombinant adenovirus of amended claim 36 in the present application were non-obvious over the combination of Steg I and Ohno because there was no reasonable expectation that the method would work. Applicants assert that if there was no reasonable expectation that the claimed compositions could be used successfully in the method claims of the parent

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case, there could be no motivation to make the proposed combination of Steg I and Ohno.

The Examiner's assertion that the present composition claims are not patentably distinct from the method claims (claims 1-24) of the '011 patent supports this conclusion. In rejecting claims 36, 37, and 39 for obviousness-type double patenting over the claims of the '011 patent, the Examiner asserts that the present composition claims are not patentably distinct from the method claims (claims 1-24) of the issued patent, which issued over the combination of Ohno and Steg I. Logically, if the method claims were non-obvious in view of Ohno and Steg I because there was no reasonable expectation that the method would succeed, and if the present composition claims are not patentably distinct from the allowed method claims, then the present composition claims should also be considered non-obvious over the same Ohno and Steg I references because there could be no motivation to combine those references to make the claimed composistion.

In sum, as acknowledged by the Examiner during prosecution of the '011 patent, neither Ohno or Steg I would lead one of ordinary skill in the art to reasonably expect that compositions or catheter devices as recited in the present amended claims would be useful. Therefore, one of ordinary skill would not have been motivated to make these inventions. Accordingly, a proper obviousness rejection has not been made. Thus, Applicants respectfully request that the rejection of claims 36, 37, and 39 under 35 U.S.C. § 103 be withdrawn. As discussed above, claims 38 and 40 have been canceled and the rejection of these claims under 35 U.S.C. § 103 is moot.

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V. Double Patenting Rejections

The Examiner rejects claim 42 under 35 U.S.C. § 101 as claiming the same invention as claim 19 of the '011 patent. (*See* Office Action, p. 13). Without acquiescing in the rejection, and solely to advance prosecution, Applicants have canceled claims 41-44 without disclaimer of the subject matter contained therein. Thus, the Examiner's rejection of claim 42 for double patenting is moot.

The Examiner also rejects claims 36-41, 43, and 44 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-24 of the '011 patent. As noted previously, claims 38 and 40-44 have been canceled. Once allowable subject matter is identified, Applicants will file a terminal disclaimer to obviate the obviousness-type double-patenting rejection of claims 36, 37, and 39.

In view of the foregoing amendments and remarks, Applicants respectfully request the reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account No. 06-0916.

Respectfully submitted,

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Dated: August 29, 2003

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